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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/535,609	11/02/2007	Ian C. Bathurst	GJE-7631	7257

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EXAMINER	
HA, JULIE	

ART UNIT	PAPER NUMBER
1654	

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06/03/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/535,609	BATHURST ET AL.	
	Examiner	Art Unit	
	JULIE HA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 16-33* is/are pending in the application.

4a) Of the above claim(s) *1-12,16-22 and 32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-31, 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/2/05 and 2/5/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Election/Restriction filed on March 24, 2009 is acknowledged. Claims 13-15 have been cancelled. Claims 1-12 and 16-33 are pending in this application.

Restriction

1. Applicant's election of Group 3 (claims 23-33) and the election of keratinisation (ichthyosis) for the species of disorder in the reply filed on March 24, 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Restriction requirement is deemed proper and is made FINAL in this office action. Claims 1-12 and 16-22 are withdrawn from further consideration, pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. A search was conducted on the elected species, ichthyosis, and it appears to be free of prior art. The search was extended to other species of keraitnization and skin irritation and a prior art was found. Claim 32 is withdrawn from further consideration, as being drawn to nonelected species of the elected species and prior art found. Claims 23-31 and 33 are examined on the merits in this office action.

TRADEMARK

The use of the trademark CARBOPOL™ at paragraph [0050], PLURONIC™ at paragraph [0051], VERSAmax™ at paragraph [0102], SOFTmax® PRO at paragraph

[0103], EXCEL® at paragraph [0103], ECOSCINT® at paragraph [0107], MICROMAN® at paragraph [0109], PIPETTEMAN® at paragraph [0110], SCINTILENE® at paragraph [0111] have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Rejection

35 U.S.C. 112, 2nd

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 31 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Regarding claim 31, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Claim 31 recites “such as actinic or seborrheic keratosis” and “such as ichthyosis” at lines 5-6 of the claim.

5. Claim 31 recites parenthetical expression "(particularly lichen planus)," “(Bowen's disease),” and “(particularly lamellar ichthyosis),” at line 4, line 5 and lines 6-7, respectively. The metes and bounds of claim 31 is rendered vague and indefinite by the

parenthetical recitation of "(particularly lichen planus)," "(Bowen's disease)," and "(particularly lamellar ichthyosis)" because it is unclear as to whether the limitation is part of the instantly claimed subject matter.

35 U.S.C. 112, 1st

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 23-31 and 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of an inflammatory or hyperproliferative mucocutaneous disorder, does not reasonably provide enablement for prevention of these disorders, and enablement for treatment and prevention of all hyperproliferative diseases, such as cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature or the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are

weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention and (5) The breadth of the claims:

The invention is drawn to a method for the treatment or prevention of an inflammatory or hyperproliferative mucocutaneous disorder, the method comprising administering to a subject in need thereof an effective amount of a composition comprising a protease inhibitor and a gelling agent.

(2) The state of the prior art:

The Merck manual indicates that there are vast numbers of inflammatory disorders known. For example, pelvic inflammatory disease, inflammatory disease of intestine, liver, Neisseria gonorrhoease, and so on. Further, the Merck manual indicates that there are vast numbers of proliferative mucocutaneous disorders, including chronic mucocutaeneous candidiasis, Leishmaniasis, Paracoccidiodomycosis, Behcet's syndrome, Herpes Simplex Virus Infections and so on. The instant specification discloses that examples of hyperproliferative and inflammatory skin or mucocutaneous disorders include skin cancer, atopic dermatitis, psoriasis, and asthma due to the inflammation of the lung mucosa (see paragraph [0002] of instant specification US 2008/0095806). The instant claims recites dermatological disorder (atopic dermatitis, skin photodamage, extrinsic skin aging, skin irritation, chronic, burn and ulcer wounds, acne, psoriasis, lichen, basal or squamous cell carcinoma, Kaposi's sarcoma, keratosis,

keritinization), disorder of the ear, ocular disorder, disorder of the gastrointestinal tract, disorder of the urinary tract, otitis, conjunctivitis, colitis or intestinal cystitis.

The Merck manual indicates that atopic dermatitis is an immune-mediated inflammation of the skin, often with a significant genetic component. Prutitus is the primary symptom, skin lesions range from mild erythema to severe lichenification (see Merck manual, Atopic Dermatitis, p. 1, 1st paragraph). The Merck manual indicates that diagnosis is clinical, and is often hard to differentiate from other dermatotoses (see Merck manual, Atopic Dermatitis, p. 2, Diagnosis). The Merck manual indicates that treatment can be supportive care and involves moisturizing, body oils or emollients, and antihistamines can help relieve pruritus (see Merck manual, Atopic Dermatitis, pp. 3-4, Prognosis and Treatment).

The Merck manual indicates that burns are injuries of skin or other tissue caused by thermal, radiation, chemical, or electrical contact (see Merck manual, Burns, p. 1, 1st paragraph). Thermal burns may result from any external heat source. Radiation burns most commonly result from prolonged exposure to solar ultraviolet radiation; chemical burns may result from strong acids, strong alkalis, phenols, cresols, mustard gas, phosphorus and certain petroleum products; electrical burns result from heat generation and electroporation of cell membranes associated with massive current of electrons (see Merck manual, Burns, pp. 1-2). Diagnosis is via clinical assessment of burn extent and depth, laboratory testing and chest x-day in admitted patients (see Merck manual, Burns, pp. 4-5, Diagnosis). Treatment is IV fluids for burns, wound cleaning, dressing

and serial assessment, surgery and physical therapy, for example (see Merck manual, Burns, pp. 5-8, Treatment).

The Merck manual indicates that Kaposi's Sarcoma is a multicentric vascular tumor caused by herpesvirus type 8, and diagnosis is by biopsy (see Merck manual, Kaposi's Sarcoma, p. 1, 1st paragraph, and p. 2, Diagnosis). Furthermore, the Merck manual indicates that KS originates from endothelial cells in response to infection by human herpesvirus 8 (HHV-8) (see Merck manual, Kaposi's Sarcoma, p. 1, 2nd paragraph). The Merck manual indicates that treatment is superficial excision, cryotherapy, or electrocoagulation for superficial lesions (see Merck manual, Kaposi's Sarcoma, p. 2).

The Merck manual indicates that Bowen's disease is most common in sun-exposed areas but may arise at any location. Treatment depends on the tumor's characteristic and may involve topical chemotherapy, curettage and electrodesiccation, surfical excision, or cryosurgery (see Merck manual, Bowen Disease, p. 1).

The Merck manual indicates that squamous cell carcinoma is a malignant tumor of epidermal keratinocytes that invades the dermis usually occurring at sun-exposed areas (see Merck manual, Squamous Cell Carcinoma, p. 1, 1st paragraph). Further more, the Merck manual indicates that biopsy is essential, and differential diagnosis includes many types of benign and malignant lesions, such as basal cell carcinoma, keratoacanthoma, actinic keratosis, verruca vulgaris, and seborrheic keratosis (see Merck manual, Squamous Cell Carcinoma, p. 1, 4th paragraph). Furthermore, the Merck manual indicates that treatment is similar that for basal cell carcinoma and includes

curettage and electrodesiccation, surgical excision, cryosurgery, topical chemotherapy or radiation therapy. At times, cure is difficult (see Merck manual, Squamous Cell Carcinoma, p. 2, Treatment).

The Merck manual indicates that psoriasis is an inflammatory disease that manifests most commonly as well-circumscribed, erythematous papules and plaques covered with silvery scales. Causes are unknown, but common triggers include trauma, infection, and certain drugs (see Merck manual, Psoriasis, p. 1, 1st paragraph). The Merck manual indicates that lesions are either aysmptomatic or mildly pruitic and are most often localized on the scalp, extensor surfaces of the elbows and knees (see Merck manual, psoriasis, p. 1, Symptoms and Signs). Diagnosis is most often by clinical appearance and distribution of lesion. Treatments include emollients, salicylic acid, coal tar, anthralin, corticosteroids, retinoids, immunosuppressants immunotherapeutic agents, and light therapy (see Merck manual, Psoriasis, pp. 3-5, Diagnosis and Treatment).

The Merck manual indicates that ichthyosis is scaling and flaking of skin ranging from mild buy annoying dryness (xeroderma) to severe disfiguring disease. Diagnosis is clinical, and treatment involves emollients and sometimes oral retinoids (see Merck manual, Ichthyosis, pp. 1-3).

Merck manual indicates that conjunctivitis results from infection, allergy or irritation. Infectious conjunctivitis is most commonly viral or bacterial and is contagious. Diagnosis is clinical evaluation; the cause of conjunctivitis is suggested by clinical findings (see Merck manual, conjunctivitis, pp. 1-9). The Merck manual indicates

treatment is antibiotics, prevention of spread and treatment of symptoms (see Merck manual, conjunctivitis, pp. 2-5, Treatment).

The Merck manual indicates that ulcerative colitis is a chronic inflammatory and ulcerative disease arising in the colonic mucosa. Extraintestinal symptoms may occur and long-term risk of colon cancer is high. Diagnosis is by colonoscopy (see Merck manual, Ulcerative Colitis, p. 1, 1st paragraph). The Merck manual indicates that ulcerative colitis (UC) usually begins in the rectum, sometimes involving the entire colon. The inflammation caused by UC affects the mucosa and submucosa (see Merck manual, Ulcerative Colitis, p. 1, Pathophysiology). Symptoms include bloody diarrhea of varied intensity and duration is interspersed with asymptomatic intervals (see Merck manual, Ulcerative Colitis, pp. 1-2, Symptoms and Signs). According to the Merck manual, UC should be distinguished from Crohn's disease and from other causes of acute colitis (eg, infection, in elderly patients, ischemia). In all patients stool cultures for enteric pathogens should be obtained, and sigmoidoscopy should be performed for visual confirmation of colitis (see Merck manual, Ulcerative Colitis, pp. 2-4, Diagnosis). Treatment includes avoiding raw fruits and vegetables, milk-free diet, drugs, corticosteroids, and surgery (see Merck manual, Ulcerative Colitis, pp. 4-6, Treatment).

The Medline plus indicates that eye cancer (intraocular cancer or retinoblastoma) affect the eyeballs. Treatment for eye cancer varies by the type and by how advanced it is. It may include surgery, radiation therapy, freezing or heat therapy, or laser surgery (see MedlinePlus, p. 1, http://www.nlm.nih.gov/medlineplus/eyecancer.html).

In regards to "preventing a cancers (hyperproliferative mucocutanoues disorder)", Merck manual indicates that cancer is an unregulated proliferation of cells due to loss of normal controls, resulting in unregulated growth, lack of differentiation, local tissue invasion, and often, metastasis. Cancer can develop in any tissue or organ at any age. Furthermore, the Merck manual indicates that many cancers are curable if detected at an early stage, and long-term remission is often possible in later stages. However, cure is not always possible and is not attempted in some advanced cases in which palliative care provides better quality of life than vigorous but fruitless attempts at tumor eradication (see Merck manual, Introduction). Additionally, the Merck manual indicates that malignancy may lead to pain, wasting, neuropathy, nausea, anorexia, seizures, hypercalcemia, hyperuricemia, or obstruction…Death typically occurs as a result of sudden or progressive failure of one or multiple organ systems (see Merck manual, Clinical Aspects of Cancer). Furthermore, a complete history and physical examination may reveal unexpected clues early cancer (see Merck manual, Clinical Aspects of Cancer, Diagnosis).

Furthermore, arts indicate the difficulties in going from *in vitro* to *in vivo* for drug development for treatment of cancers. Auerbach et al (Cancer and Metastasis Reviews, 2000, 19: 167-172) indicates that one of the major problems in angiogenesis research has been the difficulty of finding suitable methods for assessing the angiogenic response. For example, the 96 well rapid screening assay for cytokinesis was developed in order to permit screening of hybridoma supernatants…*In vitro* tests in general have been limited by the availability of suitable sources for endothelial cells,

while *in vivo* assays have proven difficult to quantitate, limited in feasibility, and the test sites are not typical of the *in vivo* reality (see p. 167, left column, 1st paragraph). Gura T (Science, 1997, 278(5340): 1041-1042, encloses 1-5) indicates that "the fundamental problem in drug discovery for cancer is that the model systems are not predictive at all" (see p. 1, 2nd paragraph). Furthermore, Gura T indicates that the results of xenograft screening turned out to be not much better than those obtained with the original models, mainly because the xenograft rumors don't behave like naturally occurring tumors in humans—they don't spread to other tissues, for example (see p. 2, 4th paragraph). Further, when patient's tumor cells in Petri dishes or culture flasks and monitor the cells' responses to various anticancer treatments, they don't work because the cells simply fail to divide in culture, and the results cannot tell a researcher how anticancer drugs will act in the body (see p. 3, 7th paragraph). Furthermore, Jain RK (Scientific American, July 1994,58-65) indicates that the existing pharmacopoeia has not markedly reduced the number of deaths caused by the most common solid tumors in adults, among them cancers of the lung, breast, colon, rectum, prostate and brain (see p. 58, left most column, 1st paragraph). Further, Jain RK indicates that to eradicate tumors, the therapeutic agents must then disperse throughout the growths in concentrations high enough to eliminate every deadly cells…solid cancers frequently impose formidable barriers to such dispersion (see p. 58, bottom of the left most column continuing onto the top of the middle column). Jain RK indicates that there are 3 critical tasks that drugs must do to attack malignant cells in a tumor: 1) it has to make its way into a microscopic blood vessel lying near malignant cells in the tumor, 2) exit from the vessel into the

surrounding matrix, and 3) migrate through the matrix to the cells. Unfortunately, tumors often develop in ways that hinder each of these steps (see p. 58, bottom of right most column). Thus, the art recognizes that going from *in vitro* studies to *in vivo* studies for cancer drug developments are difficult to achieve.

The Merck manual indicates that development of asthma is multifactorial and depends on interactions between multiple susceptibility genes and environmental factors. Susceptibility genes are thought to include those of T-helper 2 cells and their cytokines (IL-4, -5, -9, and-13). Evidence implicates household and other environmental allergens in disease development in older children and adults. Air pollution is not definitively linked to disease development. Diets low in vitamins C and E and in omega-3 fatty acids have been linked to asthma, as has obesity. Asthma has also been linked to perinatal factors, such as young maternal age, Poor maternal nutritional, prematurity, low birth weight, and lack of breastfeeding (see Merck manual, Asthma, Etiology). The Merck manual also indicates that diagnosis of asthma is based on history and physical examination and is confirmed with pulmonary function tests (see Merck manual, Diagnosis). Both chronic asthma and acute exacerbations are treated by controlling the triggering factors, drug treatment, monitoring of response to treatment and disease progression, and patient education to maximize self-management of asthma (see Merck manual, Asthma, Treatment).

The art recognizes that there are vast numbers of inflammatory or hyperproliferative mucocutaneous disorders, and the treatments for these disorders, but does not provide how to determine the individuals who are susceptible to any and all

inflammatory or hyperproliferative mucocutanoues disorders. Furthermore, in regards to cancer, the art recognizes that each cancer is different and going from *in vitro* studies to *in vivo* studies for cancer drug developments are difficult to achieve,

(3) The relative skill of those in the art:

The relative skill of those in the art is high.

(4) The predictability or unpredictability of the art:

Applicant's activity is based on the determination of predicting those who are susceptible to inflammatory or hyperproliferative mucocutaneous disorders, conditions and diseases. Since the activity is based on determining the patient population that is susceptible to inflammatory or hyperproliferative mucocutaneous disorders, conditions and diseases, the predictability in the art is low. This is due to the fact that the art has recognized that there are plethora of different conditions, disorders and diseases, but does not provide how to determine the individuals who are susceptible to these disorder, condition or disease list provided by the Merck manual. For example, not everyone suffers from ulcerative colitis, conjunctivitis, ichthyosis and so on.

As described above, The Merck manual indicates that there are vast numbers of inflammatory disorders known. For example, pelvic inflammatory disease, inflammatory disease of intestine, liver, Neisseria gonorrhoease, and so on. Further, the Merck manual indicates that there are vast numbers of proliferative mucocutaneous disorders, including chronic mucocutaeneous candidiasis, Leishmaniasis, Paracoccidiodomycosis,

Behcet's syndrome, Herpes Simplex Virus Infections and so on. The instant specification discloses that examples of hyperproliferative and inflammatory skin or mucocutaneous disorders include skin cancer, atopic dermatitis, psoriasis, and asthma due to the inflammation of the lung mucosa (see paragraph [0002] of instant specification US 2008/0095806). The instant claims recites dermatological disorder (atopic dermatitis, skin photodamage, extrinsic skin aging, skin irritation, chronic, burn and ulcer wounds, acne, psoriasis, lichen, basal or squamous cell carcinoma, Kaposi's sarcoma, keratosis, keritinization), disorder of the ear, ocular disorder, disorder of the gastrointestinal tract, disorder of the urinary tract, otitis, conjunctivitis, colitis or intestinal cystitis.

The Merck manual indicates that atopic dermatitis is an immune-mediated inflammation of the skin, often with a significant genetic component. Prutitus is the primary symptom, skin lesions range from mild erythema to severe lichenification (see Merck manual, Atopic Dermatitis, p. 1, 1st paragraph). The Merck manual indicates that diagnosis is clinical, and is often hard to differentiate from other dermatotoses (see Merck manual, Atopic Dermatitis, p. 2, Diagnosis). The Merck manual indicates that treatment can be supportive care and involves moisturizing, body oils or emollients, and antihistamines can help relieve pruritus (see Merck manual, Atopic Dermatitis, pp. 3-4, Prognosis and Treatment).

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most commonly result from prolonged exposure to solar ultraviolet radiation; chemical burns may result from strong acids, strong alkalis, phenols, cresols, mustard gas, phosphorus and certain petroleum products; electrical burns result from heat generation and electroporation of cell membranes associated with massive current of electrons (see Merck manual, Burns, pp. 1-2). Diagnosis is via clinical assessment of burn extent and depth, laboratory testing and chest x-day in admitted patients (see Merck manual, Burns, pp. 4-5, Diagnosis). Treatment is IV fluids for burns, wound cleaning, dressing and serial assessment, surgery and physical therapy, for example (see Merck manual, Burns, pp. 5-8, Treatment).

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In regards to "preventing a cancers (hyperproliferative mucocutanoues disorder)", Merck manual indicates that cancer is an unregulated proliferation of cells due to loss of normal controls, resulting in unregulated growth, lack of differentiation, local tissue invasion, and often, metastasis. Cancer can develop in any tissue or organ at any age. Furthermore, the Merck manual indicates that many cancers are curable if detected at an early stage, and long-term remission is often possible in later stages. However, cure is not always possible and is not attempted in some advanced cases in which palliative care provides better quality of life than vigorous but fruitless attempts at tumor eradication (see Merck manual, Introduction). Additionally, the Merck manual indicates that malignancy may lead to pain, wasting, neuropathy, nausea, anorexia, seizures, hypercalcemia, hyperuricemia, or obstruction…Death typically occurs as a result of sudden or progressive failure of one or multiple organ systems (see Merck manual, Clinical Aspects of Cancer). Furthermore, a complete history and physical examination may reveal unexpected clues early cancer (see Merck manual, Clinical Aspects of Cancer, Diagnosis).

Furthermore, arts indicate the difficulties in going from *in vitro* to *in vivo* for drug development for treatment of cancers. Auerbach et al (Cancer and Metastasis Reviews, 2000, 19: 167-172) indicates that one of the major problems in angiogenesis research has been the difficulty of finding suitable methods for assessing the angiogenic response. For example, the 96 well rapid screening assay for cytokinesis was developed in order to permit screening of hybridoma supernatants…*In vitro* tests in general have been limited by the availability of suitable sources for endothelial cells, while *in vivo* assays have proven difficult to quantitate, limited in feasibility, and the test sites are not typical of the *in vivo* reality (see p. 167, left column, 1st paragraph). Gura T (Science, 1997, 278(5340): 1041-1042, encloses 1-5) indicates that "the fundamental problem in drug discovery for cancer is that the model systems are not predictive at all" (see p. 1, 2nd paragraph). Furthermore, Gura T indicates that the results of xenograft screening turned out to be not much better than those obtained with the original models, mainly because the xenograft rumors don't behave like naturally occurring tumors in humans—they don't spread to other tissues, for example (see p. 2, 4th paragraph). Further, when patient's tumor cells in Petri dishes or culture flasks and monitor the cells' responses to various anticancer treatments, they don't work because the cells simply fail to divide in culture, and the results cannot tell a researcher how anticancer drugs will act in the body (see p. 3, 7th paragraph). Furthermore, Jain RK (Scientific American, July 1994,58-65) indicates that the existing pharmacopoeia has not markedly reduced the number of deaths caused by the most common solid tumors in adults, among them cancers of the lung, breast, colon, rectum, prostate and brain (see p. 58, left most

column, 1st paragraph). Further, Jain RK indicates that to eradicate tumors, the therapeutic agents must then disperse throughout the growths in concentrations high enough to eliminate every deadly cells…solid cancers frequently impose formidable barriers to such dispersion (see p. 58, bottom of the left most column continuing onto the top of the middle column). Jain RK indicates that there are 3 critical tasks that drugs must do to attack malignant cells in a tumor: 1) it has to make its way into a microscopic blood vessel lying near malignant cells in the tumor, 2) exit from the vessel into the surrounding matrix, and 3) migrate through the matrix to the cells. Unfortunately, tumors often develop in ways that hinder each of these steps (see p. 58, bottom of right most column). Thus, the art recognizes that going from *in vitro* studies to *in vivo* studies for cancer drug developments are difficult to achieve.

The Merck manual indicates that development of asthma is multifactorial and depends on interactions between multiple susceptibility genes and environmental factors. Susceptibility genes are thought to include those of T-helper 2 cells and their cytokines (IL-4, -5, -9, and-13). Evidence implicates household and other environmental allergens in disease development in older children and adults. Air pollution is not definitively linked to disease development. Diets low in vitamins C and E and in omega-3 fatty acids have been linked to asthma, as has obesity. Asthma has also been linked to perinatal factors, such as young maternal age, Poor maternal nutritional, prematurity, low birth weight, and lack of breastfeeding (see Merck manual, Asthma, Etiology). The Merck manual also indicates that diagnosis of asthma is based on history and physical examination and is confirmed with pulmonary function tests (see Merck manual,

Diagnosis). Both chronic asthma and acute exacerbations are treated by controlling the triggering factors, drug treatment, monitoring of response to treatment and disease progression, and patient education to maximize self-management of asthma (see Merck manual, Asthma, Treatment).

The Applicant has not shown who will be susceptible to these disorder, condition or disease. There are too many variables between the patient populations, thus, it clearly shows the unpredictability of the art. In regards to treating and preventing cancer, the art recognizes that going from *in vitro* studies to *in vivo* studies for cancer drug developments are difficult to achieve, therefore, it clearly shows the unpredictability of the art.

(6) The amount of direction or guidance presented and (7) The presence or absence of working examples:

Although the specification provides guidance on how to make the compounds and administer the compound, it is unclear as to when to administer the compound and the patient population. The specification describes the in vitro absorption of nine topical alpha 1-antitrypsin gel formulations in intact human cadaver skin (see paragraph [0105] of instant specification, US 2008/0095806 A1). The specification describes application of drug to the human cadavar skin, and the samples were placed in a scintillation vial. The specification describes tape stripping (stratum corneum) of the skin. The first two strips remove the excess drug adhering to the outher surface of the stratum corneum were counted. The specification describes that the amount of alpha 1-antitrypsin

recovered in the reservoir, washes, gauze wipes, and skin compartments (stratum corneum, epidermis, dermis) was determined by calculating the amount of the total applied DPM recovered in the respective compartments (see Example 2).

The specification has not provided guidance in the way of a disclosure to how to determine individuals that need protection against any and all inflammatory or hyperproliderative mucocutaneous disorder, condition or disease, including dermatological disorder, disorder of the ear, ocular disorder, disorder of the gastrointestinal tract or disorder of the urinary tract. The specification does not provide any guidance as when to administer the composition to prevent an inflammatory or hyperproliferative mucocutaneous disorder. There is no working example as to a treatment or prevention of an inflammatory or hyperproliferative mucocutanoues disorder.

There is no clear guidance as to how to determine the patient population, since not all people suffer from the same disorder, condition or disease. Since art recognizes that there are countless different conditions, disorders and diseases, but does not provide how to determine the individuals who are susceptible to any disorder, condition or disease, and that these diseases must have clinical diagnosis, more guidance is necessary.

(8) The quantity of experimentation necessary:

In order to treat a disease, a dosage, the subject and regimen must be identified. In order to ameliorate a disease symptoms or conditions, the end point of the treatment

also needs to be identified. Since it is uncertain to predict the patient population who are susceptible for inflammatory or hyperproliferative mucocutanoues disorder, condition or disease, and the Applicant have not provided the appropriate time frame at which the compound should be administered, one of ordinary skill in the art would be burdened with undue "painstaking experimentation study" to determine if the compound would be effective in treating an adult, child, or an infant from all disorder, condition or disease.

Please note that the term "prevent" in an absolute definition which means to stop from occurring and, thus, requires a higher standard for enablement than does "therapeutic" or "treat" or "alleviate", especially since it is notoriously well accepted in the medical art that the vast majority of afflictions/disorders suffered by mankind cannot be totally prevented with current therapies (other than certain vaccination regimes)-including preventing such disorders as inflammatory or hyperproliferative mucocutanoues disorder, such as asthma, dermatological disorders, and cancer for example, which are clearly not recognized in the medical art as being totally preventable condition.

8. Claims 23, 25-27, 29-31 and 33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude

that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP 2163.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In Regents of the University of California v. Eli Lilly & Co., the court stated:

"A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials. Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . ."). Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. The MPEP does state that for generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP 2163. Although the MPEP does not define what constitute a sufficient number of representative, the Courts have indicated what do not constitute a representative number species to adequately describe a broad generic. In Gostelli, the Court determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872 F.2d at 1012, 10 USPQ2d at 1618.

In the instant case, the claims are drawn to a method for the treatment of prevention of an inflammatory or hyperproliferative mucocutanoues disorder, wherein said method comprises administering to a subject in need thereof an effective amount of a composition comprising a protease inhibitor and a gelling agent. Claim 29 further is drawn to wherein the composition further comprises one or more pharmaceutically active agents. The generic statements protease inhibitor and pharmaceutically active agents do not provide ample written description for the compounds since the claims do not describe a single structural feature. The specification does not clearly define or provide examples of what qualify as compounds of the claimed invention.

As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is

unquestionable claims 23 and 29 are broad generics with respect all possible compounds encompassed by the claims. The possible structural variations are limitless to any class of compounds, small molecules, synthetic compounds, peptide or a peptide-like molecule that make up the class of protease inhibitors and pharmaceutically active agents. It must not be forgotten that the MPEP states that if a peptide is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds beyond compounds disclosed in the examples in the specification. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of derivatives. The specification is void of organic molecules that functions as a peptide-like molecule that qualify for the functional characteristics claimed as a peptide or a peptide-like molecule or other peptidic molecules, amino acid mimetics, peptidomimetics, and other synthetic peptide or peptide-like molecule or small molecules that can function as protease inhibitors or pharmaceutically active agents.

The specification discloses that "the protease inhibitor in the composition described herein is a serine protease inhibitor. Most preferably, the protease inhibitor is an alpha 1-antitrypsin (see paragraph [0016] of instant specification US 2008/0095806 A1). The specification further discloses that "the alpha 1-antitrypsin in the composition is

a natural protein, isolated protein, synthetic protein, recombinant protein, modified protein, biologically active fragment, substantially homologous protein, oligopeptide, homodimer, heterodimer, variants of the protein, derivative, analog, fusion protein, or agonist of alpha 1-antitrypsin" (see paragraph [0017] of instant specification as described above). The specification further discloses "protease inhibitors useful in the composition generally include but are not limited to aspartyl protease inhibitors, cysteine protease inhibitors, metalloprotease inhibitors, serine protease inhibitors, alpha 1-antitrypsin, alpha 1-antichymotrypsin, secretory leukocyte protease inhibitor and so on (see paragraph [0030] of instant specification, as described above). Furthermore, the specification discloses that “the protease inhibitor includes peptide fragments, biologically active fragments, substantially homologous polypeptides, oligopeptide, homodimers, heterodimers, variants of the polypeptides, modified polypeptides, derivatives, analogs, fusion proteins, or agonists of the polypeptide of a protease inhibitor (see paragraph [0031] of instant specification). The specification discloses that “the term biologically active fragment of a protease inhibitor refers to fragments exhibiting activity similar, but not necessarily identical, to the activity of one or more of the protease inhibitors described herein (see paragraph [0035] of instant specification). The specification describes that “pharmaceutically active agents useful in the composition include, without limitation, conticosteroids such as, for example, hydroxytiamcinolone…” (see paragraph [0053] of instant specification as described above), “…antibiotics, cytotoxic drugs, antivirals, anti-inflammatory drugs (i.e.,

salicylates, colchicine, para-aminophenol)…" (see paragraph [0054] of instant specification).

The working example describes the protease inhibitor antitrypsin and propylene glycol, glycerin, benzyl alcohol, methylparaben, propylparaban, hydroxyethyl cellulose, carbopol 980, 400 mM phosphate/citrate buffer, NaOH and purified water composition (see Table 1). The working example only describes the serine protease inhibitor alpha 1-antitrypsin in the composition. The working example does not describe any other protease inhibitor in the composition, along with any other pharmaceutically active agent. Pharmaceutically active agent can be any compound that has pharmaceutical activity, such as interferon (see US Patent No. 4,680,175) or other peptides or protein (insulin, calcitonin, GLP-1, and so on). Description of broad genus of aspartyl protease inhibitors, cysteine protease inhibitors, metalloprotease inhibitors, serine protease inhibitors, alpha 1-antitrypsin, alpha 1-antichymotrypsin, secretory leukocyte protease inhibitor for protease inhibitor and broad genus of pharmaceutically active agents such as corticosteroids, antibiotics, cytotoxic drugs, antivirals, anti-inflammaotry drugs (i.e., salicylates, colchicine, para-aminophenol is not sufficient to encompass numerous other proteins, compounds, synthetic molecules, small compounds that belong to the same genus of protease inhibitors and pharmaceutically active agents. For example, there are varying lengths, varying amino acid compositions, and numerous distinct qualities that make up the genus. For example, for antiviral agents, there are vast numbers of peptide antivirals. Schlesinger et al (US Patent No. 5,026,686) teaches antiviral peptides that have a sequence of about 4 to 10 amino acids (see columns 3-6 and claims). Hahn

patent (US Patent No. 4,816,449) teaches anti-inflammatory peptides of the formula A-B-C-D-E, having different sequences (see columns 12-14 and claims, for example). Additionally, the protease inhibitors recognize and inhibit different and distinct proteases and have varying lengths and amino acid sequences that make up the genus protease inhibitors. There is not sufficient amount of examples provided to encompass the numerous characteristics of the whole genus claimed.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate"). Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

35 U.S.C. 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 23-31 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Estis et al (US Patent No. 4,680,175).

11. Estis et al teach an interferon preparation to be administered topically comprising a therapeutically effective amount of one or more interferons, a vehicle base (prepared from a mixture of polyethylene glycol or includes hydroxyethyl cellulose) compatible with the interferon or interferons being administered, an effective amount of one or more protease inhibitors, and an effective amount of one or more anti-microbial agents (see abstract). The reference teaches that for eye diseases and diseases like herpes genitalis, herpes labialis, herpes zoster and adenovirus induced keratitis and condyolma, all of which produce skin lesions, local topical application is the preferred method of administration (see column 1, lines 52-57). The reference teaches that the patient is human (see column 4, lines 28-35, for example), meeting the limitation of claim 33. The reference further teaches that the protease inhibitors are selected from group consisting of alpha-1-antitrypsin inhibitor, alpha-2-macroglobulin, soybean inhibitor (see column 3, lines 17-25 and claim 2), and that the protease inhibitor is human alpha-1-antitrypsin inhibitor (see claim 3), meeting the limitation of claims 24 and 28. The reference teaches that in the case of vehicles in ointment, pastes, creams gels and the like, particularly preferred vehicle are those which include hydroxyethyl cellulose or are prepared from a mixture of polyethylene glycols (see column 3, lines 30-35, Example 4, claim 6), meeting the limitation of claim 27. The reference teaches interferon preparation, which meets the limitation of pharmaceutically active agents of claim 29. The reference teaches that the ointment activity is measured by placing the

ointment in a suitable container and sterile phosphate buffered saline (pH 7.4) was added to the container (see column 9, lines 14-18), meeting the limitation of claims 25-26. The claim and the instant specification do not define what is an "effective amount of a composition comprising a protease inhibitor and a gelling agent". Therefore, any effective amount meets the limitation of the claim. Furthermore, skin lesions lead to skin irritation, this further meets the limitation of claim 31. Please note, the reference teaches eye diseases (ocular disorder), the nonelected species. Therefore, the reference anticipates claims 23-31 and 33.

12. Claims 23-24, 27-28, 30-31 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Lezdey et al (US Patent No. 6,096,327, issued Aug. 1, 2000), as evidenced by Diseases of the Epidermis (https://atlases.muni.cz/atlases/kuze/atl_en/main+nenadory+epidpor.html).

13. Lezdey et al teach cosmetic compositions and method for revitalizing the skin especially where it is placed in an environment which can cause injury to the skin. The composition comprise an effective amount of a protease inhibitor for repairing effect (see abstract). The reference teaches a method for revitalizing skin and reducing wrinkles in the skin in human which comprises topically administering a compound containing an effective amount of human serine protease inhibitor (see claim 1), wherein the protease inhibitor is alpha 1-antitrypsin (see claims 5 and 6), in a suitable cosmetic carrier (see claim 8), meeting the limitation of claims 23-24 and 28. The reference further teaches that the composition contains at least 0.5 percent by weight of

the protease inhibitor (see claim 2). The reference teaches that the topical cosmetic composition is for prophylactic against skin irritations or degradation (see column 1, lines 49-57), meeting the limitation of claims 30-31. The reference teaches that as hydrophilic gelling agent, polysaccharides such as hydroxypropylcellulose is used (see column 4, lines 1-2), meeting the limitation of claim 23 in part, and 27. The instant claims and the specification do not define what an effective amount of protease inhibitor and a gelling agent is. Therefore, any effective amount meets the limitation of the claim. The reference teaches that shampoo comprising the alpha 1-antitrypsin is useful in the treatment of scalp inflammation or itch…for sensitive scalps which have sensations of purities, that is to say by itching or prickling to different factors, such as inflammation triggered by local factors such as soaps, surfactants, erythema, and the like (see column 7, lines 14-19), reading on psoriasis, skin irritation of claim 31 for example. As evidenced by Diseases of the Epidermis, Psoriasis and Ichthyosis belong to the same family of hyperkeratosis (diseases of the epidermis). Therefore, the reference anticipates instant claims 23-24, 27-28, 30-31 and 33.

35 U.S.C. 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 23-24, 27-31 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lezdey et al (US Patent No. 6,096,327), as evidenced by Diseases of Epidermis (https://atlases.muni.cz/atlases/kuze/atl_en/main+nenadory+epidpor.html) in view of Lezdey (WO 92/06706, filed with IDS).

18. Lezdey et al teach cosmetic compositions and method for revitalizing the skin especially where it is placed in an environment which can cause injury to the skin. The composition comprise an effective amount of a protease inhibitor for repairing effect (see abstract). The reference teaches a method for revitalizing skin and reducing

wrinkles in the skin in human which comprises topically administering a compound containing an effective amount of human serine protease inhibitor (see claim 1), wherein the protease inhibitor is alpha 1-antitrypsin (see claims 5 and 6), in a suitable cosmetic carrier (see claim 8), meeting the limitation of claims 23-24 and 28. The reference further teaches that the composition contains at least 0.5 percent by weight of the protease inhibitor (see claim 2). The reference teaches that the topical cosmetic composition is for prophylactic against skin irritations or degradation (see column 1, lines 49-57), meeting the limitation of claims 30-31. The reference teaches that as hydrophilic gelling agent, polysaccharides such as hydroxypropylcellulose is used (see column 4, lines 1-2), meeting the limitation of claim 23 in part, and 27. The instant claims and the specification do not define what an effective amount of protease inhibitor and a gelling agent is. Therefore, any effective amount meets the limitation of the claim. The reference teaches that shampoo comprising the alpha 1-antitrypsin is useful in the treatment of scalp inflammation or itch…for sensitive scalps which have sensations of purities, that is to say by itching or prickling to different factors, such as inflammation triggered by local factors such as soaps, surfactants, erythema, and the like (see column 7, lines 14-19), reading on psoriasis, skin irritation of claim 31 for example. As evidenced by Diseases of the Epidermis, Psoriasis and Ichthyosis belong to the same family of hyperkeratosis (diseases of the epidermis). The difference between the reference and the instant claims is that the reference does not teach a composition further comprising one or more pharmaceutically active agent.

19. However, Ledzey (WO 92/06706) teaches a method of treating atopic dermatitis, including psoriasis comprising administering a therapy of inflammatory skin conditions with a composition comprising alpha 1-antitrypsin (see p. 1 and p. 3, and claims 1-3). The reference further teaches that the administration of serine protease inhibitors and combination with a corticosteroid has been found to provide a synergistic effect (see p. 6, and claim 8). The reference further teaches that alpha 1-antitrypsin has also been found especially useful in the treatment of bronchial and topical inflammatory conditions because of its association with elastase (see p. 8). The reference teaches that when topically applied, a serine protease inhibitor (alpha 1-antitrypsin) in suitable composition form is useful in the treatment of burns and inflammatory skin diseases such as psoriasis, eczema, acne and the like (see p. 9). The reference teaches the use of a non-aqueous lipid miscible carrier, such as prepared with liposomes (see p. 9, bottom paragraph).

20. Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings and add in other pharmaceutically active agents in the composition for the treatment of inflammation. One of ordinary skill in the art would be motivated to combined, since WO 92/06706 teaches that there is a synergistic effect when corticosteroid was combined with alpha 1-antitrypsin. There is a reasonable expectation of success, since both references teach treatment of skin inflammation and disorder comprising administering a composition comprising alpha 1-antitrypsin, combining a pharmaceutically active agent that is known for treating inflammation would at least give an additive effect. Furthermore, WO 92/06706 teaches synergistic effect,

thus one of ordinary skill in the art would at least expect more than an additive effect when corticosteroid is added to the composition. Furthermore, the MPEP states the following: "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.). See also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) (Claims directed to a method and material for treating cast iron using a mixture comprising calcium carbide and magnesium oxide were held unpatentable over prior art disclosures that the aforementioned components individually promote the formation of a nodular structure in cast iron.); and Ex parte Quadranti, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992) (mixture of two known herbicides held prima facie obvious). But see In re Geiger, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987) ("Based upon the prior art and the fact that each of the three components of the composition used in the claimed method is conventionally employed in the art for treating cooling water systems, the board held that it would have been prima facie obvious, within the meaning of 35 U.S.C. 103, to employ these components in combination for their known functions and to optimize the amount of each additive....Appellant argues... hindsight reconstruction or at best,... obvious to try'.... We agree with appellant."). Therefore, one of ordinary skill in the art would be motivated to

add in other pharmaceutically active agents (such as anti-inflammatory agent) that are known to treat inflammation for the treatment of for example psoriasis, since it would at least give an additive effect. One of ordinary skill in the art would at least expect an additive effect of treatment.

Conclusion

21. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Julie Ha/
Examiner, Art Unit 1654